

Klippel-Feil syndrome is clinically characterized by a short neck, low posterior hairline and limited neck movement.

Conclusions: The present study provides sufficient evidence that KFS is caused by a mutation in the MEOX1 and GDF3,GDF6 genes. This issue which has a scientific and clinical interest require an interdisciplinary approach that will ensure efficient planning of resources with involving of a performance type of management aimed to improve the situation in this category of patients as soon as possible.

Key words: cranio-vertebral anomalies, variability

285. ALDOSTERONE SYNTHASE GENE CYP11B2 -344C/T POLYMORPHISM AND GENDER ASPECTS OF ANTIHYPERTENSIVE TREATMENT EFFICACY

Susanna Tykhonova, Veronika Piskovatska, Viktoriia Iablonska

Internal Medicine Department №2, Odessa National Medical University, Odessa, Ukraine

Background. There is growing evidence that high interindividual variability in response to blood-lowering medications is partially explained by genetic factors. Multiple genes, encoding blood pressure-regulating drug receptors and receptor response mechanisms are Associated with different results in achieving target BP values under antihypertensive treatment. Despite some consistent research, showing that various genetic single-nucleotide polymorphisms (SNP) may affect antihypertensive treatment efficacy, study results in this field continue to be conflicting and provide disparate results [1]. Aldosterone is the key mineralocorticoid rennin-angiotensin-aldosterone system (RAAS) hormone, affecting distal nephron to regulate sodium resorption, excretion of potassium, and intravascular volume. So the associations between aldosterone synthase gene polymorphism and hypertension would thus be of significant interest. Studies about the potential role of aldosterone synthase gene CYP11B2 (-344T/C) polymorphism and primary hypertension demonstrated controversial results. Some results indicate that -344T/C polymorphism has an impact on hypertensive target organ damage and the response to antihypertensive drugs [2]. YP411B2 (-344T/C), studies have polymorphism is Associated with the antihypertensive response to diuretics and RAAS-inhibitors [5 □7]. Due to small study samples and controversial results, even in conditions of one population, it remains unclear, whether CYP11B2 -344T/C single-nucleotide polymorphism (SNP) affects antihypertensive

Gender-related aspects of hypertension is a research field based on physiological tendency of men to have higher BP values during the whole lifespan, regardless of race or ethnicity. Men also tend to have more modifiable risk factors, such as excessive alcohol consumption, smoking, poor diet, sedentary lifestyle, etc. [8] Highlighting mechanisms, underlying sex differences in hypertension may lead to development of tailored therapeutic strategies, adaptive to specific gender-related variables, thus improving treatment outcomes [9 □10].

Aim. Current study aimed to evaluate gender aspects of interindividual response to antihypertensive treatment along with the role of SNP CYP11B2 -344C/T in achieving target BP levels.

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Obtained data was statistically processed with the use of STATISTICA 10.0 software (StatSoft, USA). Frequency data were analyzed by Fisher exact p method, two-tailed. P values $p < 0,05$ were considered statistically significant.



Figure 1. End-stage PCR RFLP products, electrophoresis in agarose gel.

M – DNA molecular mass marker, tracks numbered 1-15 represent corresponding DNA samples.

Results. Approximately one third (11; 33,3%) of men enrolled into the study controlled BP effectively under the treatment. Proportion of women with proper BP control was significantly higher ($p=0,03$), more than half of women (34; 56,7%) had proper office BP levels. Groups of men and women were comparable between each other according to the mean quantity of prescribed medications, type of combination, administered in order to reduce BP. Remarkably, equally men and women, who did not reach target BP levels, have had family history of early CVEs ($p=0,034$; $p=0,007$, correspondingly). Women with lack of proper BP control had significantly higher rate of concomitant type 2 diabetes mellitus, than women with target BP levels under antihypertensive treatment.

Table 1.

Risk factors	Rate among women with BP \geq 135/85 mm Hg (n=32)	Rate among men with BP \geq 135/85 mm Hg (n=23)	P
FAH, %	90,6	91,3	1
FH of premature CVE, %	37,5	39,1	1
Smoking, %	18,8	86,9	0,001
Excessive alcohol intake, %	0	43,5	0,001
Sedentary lifestyle, %	46,9	39,1	0,59
Excessive salt intake, %	50	65,2	0,28
Excessive intake of saturated and trans-fats, %	75	82,6	0,28
Obesity, %	71,9	56,5	0,26
Type 2 diabetes mellitus, %	46,9	39,1	0,59

Comparing subgroups of men and women with inadequate response to antihypertensive therapy by major cardiovascular risk factors showed that men with poor BP control have had some statistically significant differences with women, not achieving target BP levels. Men have had a current status of smoker significantly along with the excessive alcohol intake more often, than women ($p=0,001$; $p=0,001$, correspondingly).

Genotyping demonstrated, that the men were CYP11B2 -344C/T CC-genotype carriers less often, than women ($p=0,03$), while differences between gender groups regarding heterozygous genotype and TT-genotype were insignificant (see Table 2).

Table 2.

CYP11B2 haplotype	-344C/T	Female hypertensive patients (n=60)	Male hypertensive patients (n=33)	P, two-tailed, Fisher method
CC, %		28,3	9,1	0,03
CT, %		27; 45	21; 63,6	0,08
TT, %		16; 26,7	9; 27,3	0,95

Analyzing women's cardiovascular risk factors, that can have an implication in hypertension course and outcomes no statistically significant differences were found between women who properly controlled BP under treatment and those, who did not achieve BP goals. Women with CC-genotype of CYP11B2 gene demonstrated high rates of hypertension occurrence during the menopause (see Table 3).

Table 3.

Risk factors	Women with CC-genotype (n=17)	Women with TT-genotype (n=16)	P, two-tailed, Fisher method
PCOS	1 (5,9%)	1 (6,3%)	1
Gestational hypertension	5 (29,4%)	3 (18,8%)	0,688
History of preeclampsia and/or eclampsia	1 (5,9%)	1 (6,3%)	1
Surgical menopause	1 (5,9%)	1 (6,3%)	1
Hypertension in menopause	11 (64,7%)	4 (25%)	0,037

Conclusions. Thus, study results showed that proportion of men, tending to control BP levels under prescribed treatment was lower than in women. Traditional cardiovascular risk factors analysis showed an association between family history of premature cardiovascular events and improper BP control in both men and women, receiving adequate and comparable antihypertensive treatment. Comparison for the rate of cardiovascular risk factors within gender subgroups, experiencing inadequate BP control under treatment demonstrated high rates of current smokers and alcohol abuse in males. Gender groups demonstrated statistically significant difference in C-monozygous genotype rate, representing men to be T-allele carriers more often than women. Carrying CYP11B2 -344C/T CC-genotype was a factor, Associated with high rate of hypertension during the menopause, pointing towards special attention for women with certain gene-environmental interaction, regarding BP control and cardiovascular prevention.

Keywords: aldosterone synthase gene CYP11B2 -344C/T polymorphism, antihypertensive treatment, classic modifiable and non-modifiable risk factors, gender.